

Amendment to the Claims:

Please amend the claims as follows.

This listing of claims will replace all prior versions, and listing, of claims in the application:

Listing of Claims:

Claim 1 (currently amended): A method for stable transduction of primary cells of the hematopoietic system and/or hematopoietic stem cells comprising contacting the surface of said primary cell or hematopoietic stem cells at the same time *in vitro* or *ex vivo* with both a lentiviral vector and at least one molecule which binds said cell surface by binding to a cell surface receptor,

wherein at least about 75% of the cells are stably transduced after about seven to ten days, or at about 14 days

and the binding of the cell surface receptor binding molecule to the cell surface receptor does not induce apoptosis of the cell and the binding of the cell surface receptor binding molecule to the cell surface receptor results in the cell being more receptive to transduction by the lentiviral vector.

Claim 2 (currently amended): The method of claim 1 further comprising continuous contacting the primary cells or hematopoietic stem cells *in vitro* or *ex vivo* with the lentiviral vector after the simultaneous contacting of the primary cells or hematopoietic stem cells with the lentiviral vector and the at least one cell surface receptor binding molecule.

Claim 3 (currently amended): The method of claim 1 further comprising continuous contacting the primary cells or hematopoietic stem cells *in vitro* or *ex vivo* with the at least one cell surface binding molecule after the simultaneous contacting of the primary cells or hematopoietic stem cells with the lentiviral vector and the at least one cell surface receptor binding molecule.

Claim 4 (currently amended): The method of claim 1 further comprising continuous contacting the primary cells or hematopoietic stem cells *in vitro* or *ex vivo* with the lentiviral vector and the at least one cell surface binding molecule after the initial simultaneous contact of the

primary cells or hematopoietic stem cells with the lentivirus vector and the at least one cell surface receptor binding molecule.

Claim 5 (original): The method of claim 1 where said contacting with a lentiviral vector occurs more than once.

Claim 6 (previously presented): The method of claim 1 wherein said lentiviral vector is derived from a human immunodeficiency virus (HIV).

Claim 7 (currently amended): The method of claim 1 wherein said cell surface receptor binding molecule is an antibody, an antigen binding fragment, a ligand or a cell surface molecule.

Claim 8 (original): The method of claim 1 wherein said lentiviral vector comprises at least one cis-acting nucleotide sequence derived from the gag, pol, env, vif, vpr, vpu, tat or rev genes.

Claim 9 (previously presented): The method of claim 8 wherein said cis-acting nucleotide sequence is not expressed or is a fragment or a mutant of the gag, pol, env, vif, vpr, vpu, tat or rev genes.

Claim 10 (previously presented): The method of claim 1 wherein said lentiviral vector is derived from HIV-1 or HIV-2.

Claim 11 (original): The method of claim 1 wherein said lentiviral vector is a pseudotyped vector.

Claim 12 (previously presented): The method of claim 11 wherein said pseudotyped vector comprises the vesicular stomatitis virus G envelope protein.

Claim 13 (previously presented): The method of claim 1 wherein said lentiviral vector is a chimeric vector comprising HIV sequences, wherein optionally the HIV sequences comprise HIV-1 and HIV-2 sequences.

Claim 14 (previously presented): The method of claim 1 wherein said primary hematopoietic cell is a CD4 positive cell or is a hematopoietic stem cell of a CD4 positive cell.

Claim 15 (previously presented): The method of claim 1 wherein said primary cell of the hematopoietic system or hematopoietic stem cell is a lymphocyte or a precursor thereof.

Claim 16 (previously presented): The method of claim 1 wherein the primary cell of the hematopoietic system or hematopoietic stem cell is a CD4 or CD8 positive cell or a precursor thereof.

Claim 17 (previously presented): The method of claim 1 wherein said primary cell of the hematopoietic system or hematopoietic stem cell is a CD34 positive cell or a precursor thereof.

Claim 18 (currently amended): The method of claim 1 wherein said at least one cell surface receptor binding molecule comprises a molecule selected from the group consisting of an FLT-3 ligand; a TPO ligand Kit ligand; antibodies that have the same cell surface binding specificity as FLT-3, TPO, or Kit ligand; CD3 ligand; a CD28 ligand; a CD25 ligand; a CD71 ligand; a CD69 ligand; and, antibodies that have are the same cell surface binding specificity of CD3, CD25, CD28, CD69 or CD71 ligand.

Claim 19 (currently amended): The method of claim 1 wherein said at least one cell surface receptor binding molecule comprises a molecule selected from the group consisting of FLT-3 ligand, TPO ligand and Kit ligand or polypeptides or other binding molecules that have the same cell surface binding specificity as FLT-3 ligand, TPO ligand, or Kit ligand.

Claim 20 (previously presented): The method of claim 1 wherein the said primary cell or hematopoietic stem cell is a dendritic cell or a cell capable of differentiating into a dendritic cell or a precursor thereof.

Claim 21 (currently amended): The method of claim 1 wherein said at least one cell surface receptor binding molecule is selected from the group consisting of compositions comprising CD34, CD3, CD28, GM-CSF, IL-4, TNF-alpha; GM-CSF, interferon-alpha; and antibodies or other binding molecules that have the same cell surface binding specificity as CD34, CD3, CD28, GM-CSF, IL-4, and TNF-alpha; GM-CSF or interferon-alpha.

Claim 22 (currently amended): The method of claim 1, wherein said at least one cell receptor surface binding molecule is selected from the group consisting of CD3 antibodies and cell surface binding fragments thereof, CD28 antibodies and cell surface binding fragments thereof, combinations of said antibodies and cell surface binding fragments thereof, and binding molecules that have the same cell surface binding specificities as the antibodies.

Claim 23 (currently amended): The method of claim 22 wherein said at least one cell surface receptor binding molecule comprises a combination of CD3 and CD28 antibodies immobilized on a bead or a surface, wherein optionally the bead or surface comprises coated beads.

Claim 24 (previously presented): The method of claim 1 culturing the primary cells or hematopoietic stem cells under conditions conducive to growth and/or proliferation.

Claim 25 (currently amended): The method of claim 24 wherein said conditions comprise culturing or further incubation the primary cells or hematopoietic stem cells with a cell surface receptor binding molecule comprising ~~comprising~~ [[or]] a cytokine.

Claim 26 (original): The method of claim 25 wherein said cytokine is interleukin-2.

Claim 27 (original): The method of claim 24 wherein said culturing is for about seven days.

Claim 28 (currently amended): The method of claim 27 ~~[[24]]~~ wherein said culturing is for about 14 days.

Claim 29 (currently amended): The method of claim 1 wherein said contacting the surface of the primary cells or hematopoietic stem cells at the same time *in vitro* or *ex vivo* with both the lentiviral vector and cell surface receptor binding molecule further comprises (a) contacting the cell surface with a lentiviral vector ~~[[is]]~~ for about 24 hours; or, (b) step (a) and is optionally repeated at least once.

Claim 30 (currently amended): The method of claim 1 wherein the lentiviral vector is present at an MOI of less than 500, or, the cells are transduced with the vector at a multiplicity of infection (MOI) such that the copies of vector per transduced cell is from about 1 to about 100.

Claims 31 and 32 (canceled)

Claim 33 (original): The method of claim 1 wherein said contacting occurs *ex vivo*.

Claim 34 (currently amended): A method for stable transduction of primary cells of the hematopoietic system and/or hematopoietic stem cells comprising

(a) isolating ~~[[from]]~~ an individual a primary cell of the hematopoietic system and/or a hematopoietic stem cell; and

(b) contacting the primary cell or hematopoietic stem cell simultaneously *in vitro* or *ex vivo* with a lentiviral vector and an at least one molecule that physically interacts with a receptor, marker, or other recognizable moiety on the surface of the primary cell or hematopoietic stem cell,

wherein greater than about 75% of the primary cells or hematopoietic stem cells are stably transduced after about seven to ten days, or at about 14 days

and the binding of the cell surface receptor binding molecule to the cell surface receptor does not induce apoptosis of the cell and the binding of the cell surface receptor binding molecule to the cell surface receptor results in the cell being more receptive to transduction by the lentiviral vector.

Claim 35 (previously presented): The method of claim 34 further comprising continuous contacting the primary cells or hematopoietic stem cells *in vitro* or *ex vivo* with the lentiviral vector after the simultaneous contacting of the primary cells with the lentiviral vector and the at least one cell surface binding molecule.

Claim 36 (previously presented): The method of claim 34 further comprising continuous contacting the primary cells or hematopoietic stem cells *in vitro* or *ex vivo* with the at least one cell surface binding molecule after the simultaneous contacting of the a lentiviral vector and the at least one cell surface binding molecule.

Claim 37 (previously presented): The method of claim 34 further comprising continuous contacting the primary cells or hematopoietic stem cells *in vitro* or *ex vivo* with the lentiviral vector and the at least one cell surface binding molecule after the initial simultaneous contact of the lentivirus vector and the at least one cell surface binding molecule.

Claim 38 (previously presented): The method of claim 34 wherein said contacting with a lentiviral vector occurs more than once.

Claim 39 (previously presented): The method of claim 34 wherein said cells are human primary cells of the hematopoietic system and/or human hematopoietic stem cells.

Claim 40 (previously presented): The method of claim 34 wherein said cell surface binding molecule is an antibody, an antigen binding fragment, a ligand or a cell surface molecule.

Claim 41 (previously presented): The method of claim 34 wherein said lentiviral vector comprises at least one cis-acting nucleotide sequence derived from the gag, pol, env, vif, vpr, vpu, tat or rev genes.

Claim 42 (previously presented): The method of claim 41, wherein said cis-acting nucleotide sequence is not expressed or is a fragment or a mutant of the gag, pol, env, vif, vpr, vpu, tat or rev genes.

Claim 43 (previously presented): The method of claim 34 wherein said lentiviral vector is an HIV-derived vector.

Claim 44 (previously presented): The method of claim 34 wherein said lentiviral vector is a pseudotyped vector.

Claim 45 (previously presented): The method of claim 44 wherein said pseudotyped vector contains the vesicular stomatitis virus G envelope protein.

Claim 46 (previously presented): The method of claim 34 wherein said primary cell or hematopoietic stem cell is a primary human cell or a human hematopoietic stem cell.

Claim 47 (previously presented): The method of claim 34 wherein said primary cell of the hematopoietic system or hematopoietic stem cell is a CD4 positive cell.

Claim 48 (previously presented): The method of claim 34 wherein said primary cell of the hematopoietic system or hematopoietic stem cell is a lymphocyte or a precursor thereof.

Claim 49 (previously presented): The method of claim 48 wherein said lymphocyte is a CD4 or CD8 positive cell.

Claim 50 (previously presented): The method of claim 34 wherein said primary cell of the hematopoietic system or hematopoietic stem cell is a CD34 positive cell or a precursor thereof.

Claim 51 (previously presented): The method of claim 34 wherein said primary cell of the hematopoietic system is a human hematopoietic stem cell or a precursor thereof.

Claim 52 (previously presented): The method of claim 34 wherein said at least one cell surface binding molecule comprises a molecule selected from the group consisting of FLT-3 ligand; a TPO ligand; a Kit ligand; an antibody that has the same cell surface binding specificity as FLT-3, TPO, or Kit ligand; a CD3 ligand; a CD28 ligand; a CD25 ligand; a CD71 ligand; a CD69 ligand; and, an antibody that has the same cell surface binding specificity of CD3, CD25, CD28, CD69 or CD71 ligand.

Claim 53 (previously presented): The method of claim 34 wherein said at least one cell surface binding molecule comprises a molecule selected from the group consisting of FLT-3 ligand, TPO ligand and Kit ligand or polypeptides or other binding molecules that have the same cell surface binding specificity as FLT-3 ligand, TPO ligand, or Kit ligand.

Claim 54 (previously presented): The method of claim 34 wherein the said primary cell or hematopoietic stem cell is a dendritic cell or a cell capable of differentiating into a dendritic cell.

Claim 55 (previously presented): The method of claim 34 wherein said at least one cell surface binding molecule is selected from the group of compositions comprising a CD34, a CD3, a CD28, a GM-CSF, an IL-4, a TNF-alpha; a GM-CSF; an interferon-alpha; and an antibody or other binding molecule that has the same cell surface binding specificity as CD34, CD3, CD28, GM-CSF, IL-4, and TNF-alpha, GM-CSF or interferon-alpha.

Claim 56 (previously presented): The method of claim 34 wherein said at least one cell surface binding molecule is selected from the group consisting of CD3 antibodies and cell surface



binding fragments thereof, CD28 antibodies and cell surface binding fragments thereof, combinations of said antibodies and cell surface binding fragments thereof, and binding molecules that have the same cell surface binding specificities as the antibodies,

and optionally the least one cell surface binding molecule comprises at least two of the cell surface binding molecules immobilized on a bead or a surface.

Claim 57 (previously presented): The method of claim 56 wherein said at least one cell surface binding molecule comprises a combination of CD3 and CD28 antibodies immobilized on coated beads.

Claim 58 (previously presented): The method of claim 34 further comprising culturing the primary cells or hematopoietic stem cells under conditions conducive to growth and/or proliferation.

Claim 59 (previously presented): The method of claim 58 wherein said conditions comprise further incubation with a cell surface binding molecule or a cytokine.

Claim 60 (previously presented): The method of claim 59 wherein said cytokine is interleukin-2.

Claim 61 (previously presented): The method of claim 58 wherein said culturing is for about seven days.

Claim 62 (previously presented): The method of claim 58 wherein said culturing is for about 14 days.

Claim 63 (previously presented): The method of claim 34 wherein said contacting the primary cells or hematopoietic stem cells with a lentiviral vector is for about 24 hours and is optionally repeated at least once.

Claim 64 (currently amended): The method of claim 34 wherein the lentiviral vector is present at an MOI of less than 500, or, the cells are transduced with the vector at a multiplicity of infection (MOI) such that the copies of vector per transduced cell is from about 1 to about 100.

Claim 65 (canceled)

Claim 66 (previously presented): The method of claim 34 wherein said contacting occurs *ex vivo*.

Claim 67 (previously presented): The method of claim 34 wherein said lentiviral vector is derived from a human immunodeficiency virus (HIV), wherein optionally the HIV is HIV-1 or HIV-2.

Claim 68 (previously presented): The method of claim 34 wherein said lentiviral vector is a chimeric vector comprising HIV-1 and HIV-2 sequences.

Claim 69 (previously presented): The method of claim 1 or claim 34, wherein greater than 80%, 85%, 89%, 90%, 91%, 92%, 93%, 94% or 95% of the cells are stably transduced after about 14 days.

Claim 70 (previously presented): The method of claim 34 wherein the individual is infected with a human immunodeficiency virus (HIV), wherein optionally the HIV is HIV-1 or HIV-2.

Claim 71 (previously presented): The method of claim 1 or claim 34, wherein the primary cells or hematopoietic stem cells isolated from the HIV-infected individual are pre-stimulated with at least one cell surface binding molecule, and optionally the primary cells or hematopoietic stem cells are pre-stimulated with the at least one cell surface binding molecule within twenty four (24) hours prior to simultaneously contacting the primary cells or hematopoietic stem cells *in vitro* or *ex vivo* with the lentiviral vector and the at least one cell surface binding molecule.

Claims 72 to 82 (canceled)

Claim 83 (previously presented): The method of claim 1 or claim 34, wherein at least 75% of the cells remain stably transduced after about 14 days.

Claim 84 (previously presented): The method of claim 1, the cell surface binding molecule comprises a polypeptide, a lipid, a nucleic acid, a carbohydrate or an ion.

Claim 85 (previously presented): The method of claim 1 or claim 34, further comprising introducing the transduced cell into a living subject.

Claim 86 (previously presented): The method of claim 1 or claim 34, further comprising introducing the transduced cell into a tissue or an organ.

Claim 87 (previously presented): The method of claim 1 or claim 34, further comprising introducing the transduced cell into a blastocyst.

Claim 88 (currently amended): A method for stable transduction of primary cells of the hematopoietic system and/or hematopoietic stem cells [[a cell]] with a lentiviral vector comprising contacting the cell at the same time *in vitro* or *ex vivo* with a lentiviral vector and at least one cell surface receptor binding molecule, wherein the lentiviral vector is pseudotyped, wherein the pseudotyping comprises co-transfecting or co-infecting a packaging cell with both the lentiviral vector genetic material and genetic material encoding at least one envelope protein of another virus or a cell surface receptor-binding molecule,  
wherein at least about 75% of the cells are stably transduced after about seven to ten days, or at about 14 days, and optionally at least 75% of the cells remain stably transduced after about 14 days,

and the binding of the cell surface receptor binding molecule to the cell surface receptor does not induce apoptosis of the cell and the binding of the cell surface receptor binding molecule to the cell surface receptor results in the cell being more receptive to transduction by the lentiviral vector.

Claim 89 (previously presented): The method of claim 88, wherein the lentiviral vector is pseudotyped with a *Rhabdovirus*.

Claim 90 (previously presented): The method of claim 89, wherein the *Rhabdovirus* is a Vesicular Stomatitis Virus envelope G (VSV-G) protein.

Claim 91 (previously presented): The method of claim 88, wherein the transduced cell is an astrocyte, a skin fibroblast, a epithelial cell, a neuron, a dendritic cell, a lymphocyte, a cell associated with the immune response, a vascular endothelial cell, a tumor cell, a tumor vascular endothelial cell, a liver cell, a lung cell, a bone marrow cell, an antigen presenting cell, a stromal cell, an adipocyte, a muscle cell, a pancreatic cell, a kidney cell, an ovum, a spermatocyte, a cell that contributes to the germ line, an embryonic pluripotent stem cell or a progenitor cell, a blood cell, a non-nucleated cell, a platelet or an erythrocyte.

Claim 92 (previously presented): The method of claim 1 or claim 34, wherein the transduced cell is an astrocyte, a skin fibroblast, a epithelial cell, a neuron, a dendritic cell, a lymphocyte, a cell associated with the immune response, a vascular endothelial cell, a tumor cell, a tumor vascular endothelial cell, a liver cell, a lung cell, a bone marrow cell, an antigen presenting cell, a stromal cell, an adipocyte, a muscle cell, a pancreatic cell, a kidney cell, an ovum, a spermatocyte, a cell that contributes to the germ line, an embryonic pluripotent stem cell or a progenitor cell, a blood cell, a non-nucleated cell, a platelet or an erythrocyte.

Claim 93 (previously presented): The method of claim 1, claim 34, or claim 88, wherein said at least one cell surface binding molecule comprises at least two cell surface binding molecules

selected from the group consisting of an FLT-3 ligand; a TPO ligand Kit ligand; antibodies that have the same cell surface binding specificity as FLT-3, TPO, or Kit ligand; CD3 ligand; a CD28 ligand; a CD25 ligand; a CD71 ligand; a CD69 ligand; and, antibodies that have are the same cell surface binding specificity of CD3, CD25, CD28, CD69 or CD71 ligand.

Claim 94 (previously presented): The method of claim 1, wherein the at least one cell surface binding molecule comprises a polypeptide, a lipid, a nucleic acid, a carbohydrate or an ion.

Claim 95 (previously presented): The method of claim 34, wherein the at least one cell surface binding molecule comprises a polypeptide, a lipid, a nucleic acid, a carbohydrate or an ion.

Claim 96 (previously presented): The method of claim 88, wherein the at least one cell surface binding molecule comprises a polypeptide, a lipid, a nucleic acid, a carbohydrate or an ion.

Claim 97 (previously presented): The method of claim 93, wherein the at least two cell surface binding molecules comprise immobilized  $\alpha$ CD3 and  $\alpha$ CD28.

Claim 98 (previously presented): The method of claim 22, wherein the at least one cell surface binding molecule comprises at least two cell surface binding molecules immobilized on a bead or a surface.

Claim 99 (new): The method of claim 88, wherein the lentiviral vector is present at an MOI of less than 500, or, the cells are transduced with the vector at a multiplicity of infection (MOI) such that the copies of vector per transduced cell is from about 1 to about 100.